

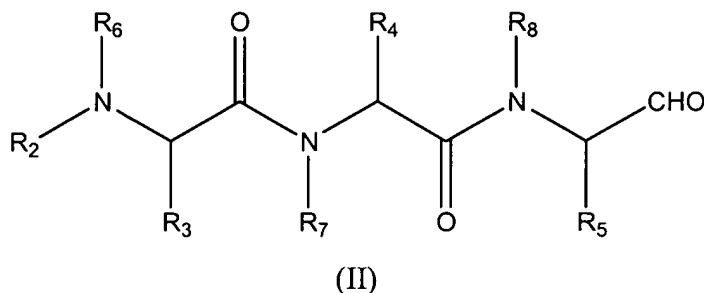
In the Claims

Please amend the claims as follows:

1. (Currently Amended) A method ~~to determine or detect an agent that alters adeno-associated virus (AAV) transduction of a mammalian cell~~, comprising:
identifying a) ~~contacting the mammalian cell with an agent~~ that enhances and adeno-associated virus; and
b) detecting or determining whether the agent alters transduction of a mammalian cell after viral binding to the cell membrane and before second strand synthesis which yields ~~to~~ an expressible form of the viral genome.
2. (Previously Presented) The method of claim 1 or 87 wherein the cell is a mammalian lung cell.
3. (Previously Presented) The method of claim 1 or 87 wherein the cell is a mammalian liver cell.
4. (Previously Presented) The method of claim 1 or 87 wherein the cell is a human cell, canine cell, murine cell, rat cell or rabbit cell.
5. (Currently Amended) The method of claim 1 or 87 wherein the transduction is enhanced before uncoating of viral particles.
6. (Previously Presented) The method of claim 1 or 87 wherein the agent enhances endosomal processing.
7. (Previously Presented) The method of claim 1 or 87 wherein the agent is an endosomal protease inhibitor.
8. (Original) The method of claim 7 wherein the agent is a cysteine protease inhibitor.

9. (Previously Presented) The method of claim 1 or 87 wherein the agent is a peptide or analog thereof.
10. (Previously Presented) The method of claim 1 or 87 wherein the virus is recombinant adeno-associated virus.
11. (Original) The method of claim 10 wherein the recombinant virus encodes a therapeutic peptide or polypeptide.
12. (Previously Presented) The method of claim 10 wherein the recombinant virus comprises a marker gene that is detectable or selectable.
- 13-28. (Cancelled)
29. (Previously Presented) The method of claim 1 or 87 wherein the agent is a compound of formula (I): $R_1-A-(B)_n-C$ wherein R_1 is an N-terminal amino acid blocking group; each A and B is independently an amino acid; C is an amino acid wherein the terminal carboxy group has been replaced by a formyl (CHO) group; and n is 0, 1, 2, or 3; or a pharmaceutically acceptable salt thereof.
30. (Original) The method of claim 29 wherein R_1 is (C_1-C_{10}) alkanoyl.
31. (Original) The method of claim 29 wherein R_1 is acetyl or benzyloxycarbonyl.
32. (Original) The method of claim 29 wherein each A and B is independently alanine, arginine, glycine, isoleucine, leucine, valine, nor-leucine or nor-valine.
33. (Original) The method of claim 29 wherein each A and B is isoleucine.

34. (Original) The method of claim 29 wherein C is alanine, arginine, glycine, isoleucine, leucine, valine, nor-leucine or nor-valine, wherein the terminal carboxy group has been replaced by a formyl (CHO) group.
35. (Original) The method of claim 29 wherein C is nor-leucine or nor-valine, wherein the terminal carboxy group has been replaced by a formyl (CHO) group.
36. (Original) The method of claim 29 wherein R₁ is (C₁-C₁₀)alkanoyl or benzyloxycarbonyl; A and B are each isoleucine; C is nor-leucine or nor-valine, wherein the terminal carboxy group has been replaced by a formyl (CHO) group; and N is 1.
37. (Previously Presented) The method of claim 1 or 87 wherein the agent is a compound of formula (II):



wherein

R₂ is an N-terminal amino acid blocking group;

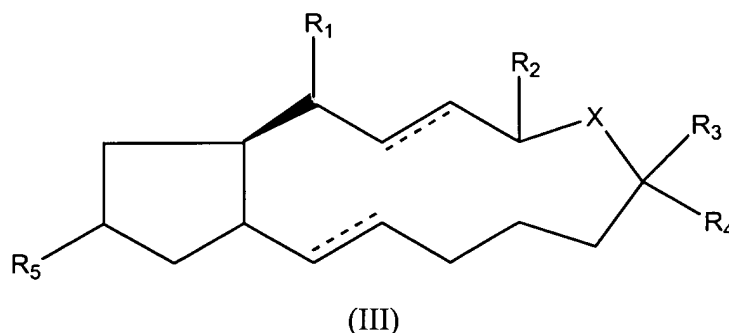
R₃, R₄, and R₅ are each independently hydrogen, (C₁-C₁₀)alkyl, aryl or aryl(C₁-C₁₀)alkyl;

and

R₆, R₇, and R₈ are each independently hydrogen, (C₁-C₁₀)alkyl, aryl or aryl(C₁-C₁₀)alkyl; or a pharmaceutically acceptable salt thereof.

38. (Original) The method of claim 37 wherein R₂ is (C₁-C₁₀)alkanoyl.
39. (Original) The method of claim 37 wherein R₂ is acetyl or benzyloxycarbonyl.
40. (Original) The method of claim 37 wherein R₃ is hydrogen or (C₁-C₁₀)alkyl.

41. (Original) The method of claim 37 wherein R_3 is 2-methylpropyl.
42. (Original) The method of claim 37 wherein R_4 is hydrogen or (C_1-C_{10}) alkyl.
43. (Original) The method of claim 37 wherein R_4 is 2-methylpropyl.
44. (Original) The method of claim 37 wherein R_5 is hydrogen or (C_1-C_{10}) alkyl.
45. (Original) The method of claim 37 wherein R_5 is butyl or propyl.
46. (Original) The method of claim 37 wherein R_2 is acetyl or benzyloxycarbonyl; R_3 and R_4 are each 2-methylpropyl; R_5 is butyl or propyl; and R_6, R_7 , and R_8 are each independently hydrogen.
47. (Previously Presented) The method of claim 1 or 87 wherein the agent is a compound of formula (III):



wherein

R_1 is H, halogen, (C_1-C_{10}) alkyl, (C_1-C_{10}) alkenyl, (C_1-C_{10}) alkynyl, (C_1-C_{10}) alkoxy, (C_1-C_{10}) alkanoyl, $(=O)$, $(=S)$, OH, SR, CN, NO_2 , trifluoromethyl or (C_1-C_{10}) alkoxy, wherein any alkyl, alkenyl, alkynyl, alkoxy or alkanoyl may optionally be substituted with one or more halogen, OH, SH, CN, NO_2 , trifluoromethyl, NRR or SR, wherein each R is independently H or (C_1-C_{10}) alkyl;

R_2 is $(=O)$ or $(=S)$;

R₃ is H, (C₁-C₁₀)alkyl, (C₁-C₁₀)alkenyl, (C₁-C₁₀)alkynyl, (C₁-C₁₀)alkoxy or (C₃-C₈)cycloalkyl, wherein any alkyl, alkenyl, alkynyl, alkoxy or cycloalkyl may optionally be substituted with one or more halogen, OH, CN, NO₂, trifluoromethyl, SR, or NRR, wherein each R is independently H or (C₁-C₁₀)alkyl;

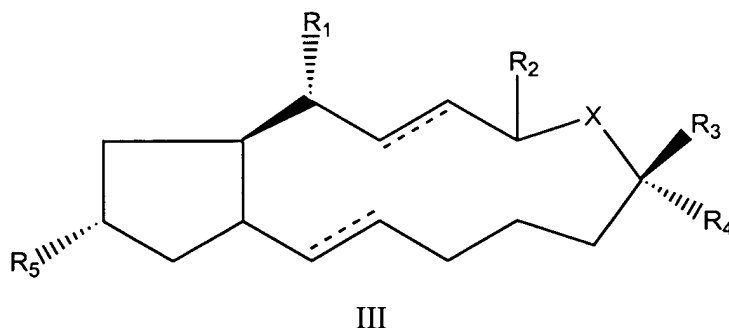
R₄ is H, (C₁-C₁₀)alkyl, (C₁-C₁₀)alkenyl, (C₁-C₁₀)alkynyl, (C₁-C₁₀)alkoxy or (C₃-C₈)cycloalkyl, wherein any alkyl, alkenyl, alkynyl, alkoxy or cycloalkyl may optionally be substituted with one or more halogen, OH, CN, NO₂, trifluoromethyl, SR, or NRR, wherein each R is independently H or (C₁-C₁₀)alkyl;

R₅ is H, halogen, (C₁-C₁₀)alkyl, (C₁-C₁₀)alkenyl, (C₁-C₁₀)alkynyl, (C₁-C₁₀)alkoxy, (C₁-C₁₀)alkanoyl, (=O), (=S), OH, SR, CN, NO₂ or trifluoromethyl, wherein any alkyl, alkenyl, alkynyl, alkoxy or alkanoyl may optionally be substituted with one or more halogen, OH, SH, CN, NO₂, trifluoromethyl, NRR or SR, wherein each R is independently H or (C₁-C₁₀)alkyl; and

X is O, S or NR wherein R is H or (C₁-C₁₀)alkyl, or a pharmaceutically acceptable salt thereof.

48. (Original) The method of claim 47 wherein R₁ is halogen, CN, NO₂, trifluoromethyl or OH.
49. (Original) The method of claim 47 wherein R₁ is OH.
50. (Original) The method of claim 47 wherein R₂ is (=O).
51. (Original) The method of claim 47 wherein R₃ is H or (C₁-C₁₀)alkyl.
52. (Original) The method of claim 47 wherein R₃ is methyl.
53. (Original) The method of claim 47 wherein R₄ is H or (C₁-C₁₀)alkyl.
54. (Original) The method of claim 47 wherein R₄ is H.

55. (Original) The method of claim 47 wherein R_5 is halogen, CN, NO_2 , trifluoromethyl or OH.
56. (Original) The method of claim 47 wherein R_5 is OH.
57. (Original) The method of claim 47 wherein X is O or S.
58. (Original) The method of claim 47 wherein X is O.
59. (Original) The method of claim 47 wherein both ----- are a single bond.
60. (Original) The method of claim 47 wherein one ----- is a double bond.
61. (Original) The method of claim 47 wherein both ----- are a double bond.
62. (Original) The method of claim 45 wherein R_1 is OH, R_2 is (=O), R_3 is methyl, R_4 is H, R_5 is OH, X is O, and both ----- are a double bond.
63. (Previously Presented) The method of claim 47 wherein the compound is a compound of formula (III):



64. (Original) The method of claim 63 wherein R_1 is halogen, CN, NO_2 , trifluoromethyl or OH.

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65. (Original) The method of claim 63 wherein R₁ is OH.
66. (Original) The method of claim 63 wherein R₂ is (=O).
67. (Original) The method of claim 63 wherein R₃ is H or (C₁-C₁₀)alkyl.
68. (Original) The method of claim 63 wherein R₃ is methyl.
69. (Original) The method of claim 63 wherein R₄ is H or (C₁-C₁₀)alkyl.
70. (Original) The method of claim 63 wherein R₄ is H.
71. (Original) The method of claim 63 wherein R₅ is halogen, CN, NO₂, trifluoromethyl or OH.
72. (Original) The method of claim 63 wherein R₅ is OH.
73. (Original) The method of claim 63 wherein X is O or S.
74. (Original) The method of claim 63 wherein X is O.
75. (Original) The method of claim 63 wherein both ----- are a single bond.
76. (Original) The method of claim 63 wherein one ----- is a double bond.
77. (Original) The method of claim 63 wherein both ----- are a double bond.
78. (Original) The method of claim 63 wherein R₁ is OH, R₂ is (=O), R₃ is methyl, R₄ is H, R₅ is OH, X is O, and both ----- are a double bond.

79. (Previously Presented) The method of claim 1 or 87 wherein the agent inhibits the activation of ubiquitin, the transfer of ubiquitin to the ubiquitin carrier protein, ubiquitin ligase, or a combination thereof.
80. (Previously Presented) The method of claim 1 or 87 wherein the agent inhibits ubiquitin ligase.
81. (Previously Presented) The method of claim 1 or 87 wherein the agent is a compound of formula (IV):
- $$R-A-A_1-R_1$$
- wherein R is hydrogen, an amino acid, or a peptide, wherein the N-terminus amino acid can optionally be protected at the amino group with acetyl, acyl, trifluoroacetyl, or benzyloxycarbonyl; A is an amino acid or a direct bond; A₁ is an amino acid; and R₁ is hydroxy or an amino acid, wherein the C-terminus amino acid can optionally be protected at the carboxy group with (C₁-C₆)alkyl, phenyl, benzyl ester or amide (e.g., C(=O)NR₂, wherein each R is independently hydrogen or (C₁-C₆)alkyl); or a pharmaceutically acceptable salt thereof.
82. (Original) The method of claim 81 wherein the agent is H-Leu-Ala-OH, H-His-Ala-OH, or a combination thereof.
83. (Previously Presented) The method of claim 1 or 87 further comprising administering a second agent that enhances the activity of the agent.
84. (Original) The method of claim 83 wherein the second agent is EGTA.
85. (Canceled)

86. (Previously Presented) The method of claim 1 or 87 wherein the agent alters endosomal processing.
87. (Currently Amended) A method to identify an agent that ~~alters~~ enhances adeno-associated virus (AAV) transduction of a mammalian cell, comprising:
- a) contacting the mammalian cell with ~~an agent~~ one or more agents and adeno-associated virus;
 - ~~b) detecting or determining whether the agent alters viral transduction; and~~
 - e) b) identifying ~~whether the~~ at least one agent ~~alters~~ that enhances transduction after viral binding to the cell membrane and before second strand synthesis ~~to~~ which yields an expressible form of the viral genome.